

Please add new claims 61-75.

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--61. (New) A Protein C or Activated Protein C polypeptide comprising a GLA domain of SEQ ID NO:1, said GLA domain having substituted and unsubstituted residues, wherein the substituted residues are one to ten substitutions at residues selected from the group consisting of residues 2, 5, 9, 11, 12, 29, 33, 34, 35 and 36, and wherein the unsubstituted residues correspond to SEQ ID NO:1, provided that if position 33 is substituted with γ -carboxyglutamic acid, at least one additional substitution is made at position 2, 5, 9, 11, 12, 29, 34, 35, or 36.

62. (New) The polypeptide of claim 61, wherein said polypeptide is an active site modified activated protein C.

63. (New) A pharmaceutical composition comprising the polypeptide of claim 61 and a pharmaceutically acceptable carrier.

64. (New) A method of treating a patient in need thereof, which comprises administering to said patient the pharmaceutical composition of claim 63.

65. (New) The method of claim 64, which further comprises administering an anticoagulant agent.

66. (New) The method of claim 65, wherein said anticoagulant agent is aspirin, warfarin, or heparin.

67. (New) A protein C or activated protein C polypeptide comprising a GLA domain of SEQ ID NO:1, said GLA domain having substituted and unsubstituted residues, wherein the substituted residues are one to ten substitutions at residues selected from the group consisting of residues 2, 5, 9, 11, 12, 29, 33, 34, 35, and 36, and wherein the unsubstituted residues correspond to SEQ ID NO:1, provided that if position 33 is substituted, at least one additional substitution is made at position 2, 5, 9, 11, 12, 29, 34, 35, or 36.

68. (New) The polypeptide of claim 67, wherein said polypeptide is an active site modified activated protein C.

69. (New) A pharmaceutical composition comprising the polypeptide of claim 67 and a pharmaceutically acceptable carrier.

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and
70. (New) A method of treating a patient in need thereof, which comprises administering to said patient the pharmaceutical composition of claim 69.

71. (New) The method of claim 70, said method further comprising administering an anticoagulant agent.

72. (New) The method of claim 71, wherein said anticoagulant agent is aspirin, warfarin, or heparin.

73. (New) A Protein C or Activated Protein C polypeptide comprising a GLA domain, said GLA domain having at least one amino acid substitution at residues selected from the group consisting of residues 11, 12, 33 and 34, and at least one additional amino acid substitution at residues selected from the group consisting of residues 2, 5, 9, 11, 12, 29, 33, 34, 35 and 36, wherein said amino acid substitutions enhance membrane binding affinity of said polypeptide relative to a protein C or activated protein C polypeptide having the GLA domain of SEQ ID NO:1, wherein said GLA domain comprises at least 35 unsubstituted residues, and wherein all of said unsubstituted residues correspond to the amino acid sequence of SEQ ID NO:1.

74. (New) A Protein C or Activated Protein C polypeptide comprising a GLA domain, said GLA domain having at least one amino acid substitution at residues selected from the group consisting of residues 11, 12, 33 and 34, and at least one additional amino acid substitution at residues selected from the group consisting of residues 2, 5, 9, 11, 12, 29, 33, 34, 35 and 36, wherein said amino acid substitutions enhance membrane binding affinity of said polypeptide

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Page : 4

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Conclude

relative to a protein C or activated protein C polypeptide having the Gla domain of SEQ ID NO:1, wherein said GLA domain has no more than 10 substituted residues, and wherein all unsubstituted residues of said Gla domain correspond to the amino acid sequence of SEQ ID NO:1.

75. (New) The polypeptide of claim 74, wherein said amino acid substitutions enhance activity of said polypeptide relative to a protein C or activated protein C polypeptide having the Gla domain of SEQ ID NO:1.--
